An Efficient Asymmetric Synthesis of Tarchonanthuslactone

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Dedicated to Professor Manfred T. Reetz on the occasion of his 60th birthday

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An efficient and straightforward ten-step asymmetric synthesis of the polyketide tarchonanthuslactone (**1**) in good overall yield (21% starting from chloro lactone **5**) and with excellent diastereomeric and enantiomeric excesses (*de*, *ee* ≥ 96%) is described. The new synthetic route is based on the α,β-unsaturated δ-lactone building block **5**, available in enantiopure form (*ee* > 99%) through an enzymatic procedure, and its conversion into methyl ketone **11** by an Umpolung strategy.

Introduction

Many natural products with different biological activities, such as antitumour, antibacterial, antifungal or immunosuppressive properties, possess α,β-unsaturated δ-lactone moieties as an important structural feature. The α,β-unsaturated δ-lactone functionality is presumed to be responsible for the biological activities, due to its ability to act as a Michael acceptor, enabling these molecules to bind to a target enzyme.

One of these natural products, tarchonanthuslactone (**1**), was isolated by Bohlmann in 1979 from the leaves of a tree called *Tarchonanthus trilobus*.[1] Later, Nakata and co-workers were able to assign the compound's absolute configuration by carrying out the first asymmetric synthesis of tarchonanthuslactone (**1**),[2a] and Hsu et al. found that **1** lowers the plasma glucose levels in diabetic rats as an important biological activity.[3] This important activity and the potential to transfer this application to human beings made tarchonanthuslactone (**1**) a challenging target of several total syntheses.[2a−2f]

With regard to the common structural feature in a number of bioactive natural products, the development of new synthetic strategies towards this α,β-unsaturated δ-lactone moiety should open up access to several natural products, such as tetrahydrolipstatin,[4] (+)-strictifolione,[5] fostriecin,[6] or the cryptocarya family.[7] With the development of an efficient asymmetric synthesis of both enantiomers of 6-chloromethyl-5,6-dihydropyran-2-one (**5**), a synthetic equivalent of the lactone moiety could be provided.[8] The versatility of the δ-lactone building block **5** has already been demonstrated by us in the total syntheses of the natural products (*S*)-argentilactone, (*S*)-goniothalamin,[9] and callystatin A.[10] Here we report an efficient, diastereo- and enantioselective synthesis of the title natural product tarchonanthuslactone (**1**) from the versatile δ-lactone building block **5**.

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Results and Discussion

Our retrosynthetic analysis of tarchonanthuslactone (**1**) is shown in Scheme 1. The target molecule can be divided into the chiral alcohol **2** and the aromatic acid **3** by saponification of the ester functionality. The secondary alcohol **2** should be accessible by a *syn*-selective reduction of methyl ketone **4**, which should in turn be available from chloro lactone **5**. The aromatic acid **3** can be easily prepared from caffeic acid by application of standard hydrogenation and protection procedures.

It has recently been demonstrated that the NADP-dependent alcohol dehydrogenase of *Lactobacillus brevis* (*rec*LBADH) can be utilised for the regio- and enantioselective reduction of the 5-keto functionality of *tert*-butyl 6-chloro-3,5-dioxohexanoate (**6**).[8] After a second reduction of the carbonyl group at the 3-position, cyclisation and dehydration could be accomplished by treatment with *p*-toluenesulfonic acid (*p*TsOH) to furnish the α,β-unsaturated chloro lactone **5**. The enantiomeric chloro lactone *ent*-**5** can also be synthesized in good yield and with a very good enantiomeric excess of 94% by use of the same methodology, but in the presence of baker's yeast as biocatalyst for the reduction step (Scheme 2).[8] The enantiomeric excesses of compounds **5** and *ent*-**5** were determined by analytical HPLC on a chiral stationary phase.

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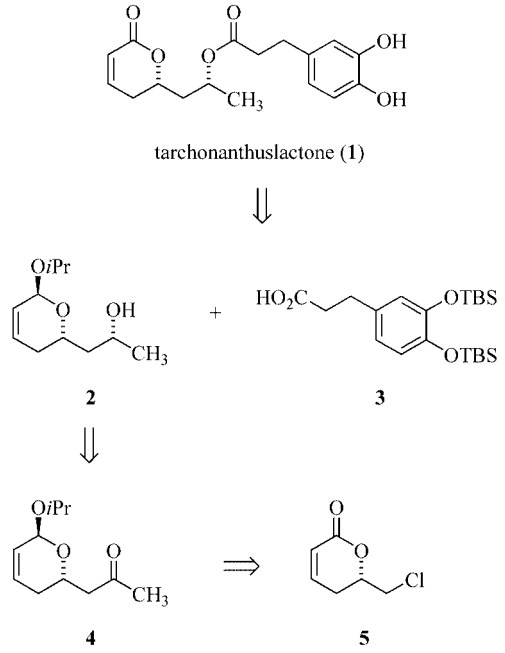
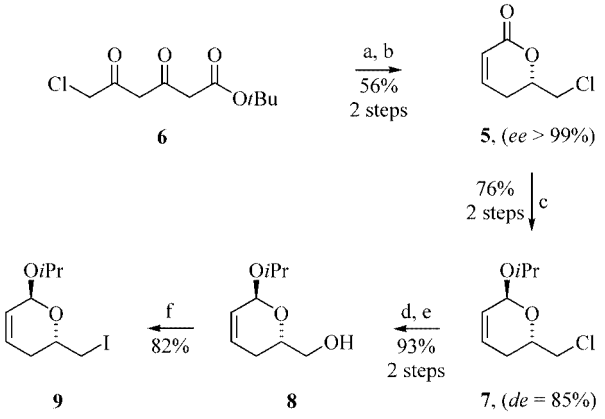


Scheme 1. Retrosynthetic analysis of tarchonanthuslactone (**1**)



Scheme 2. Reagents: (a) *rec*LBADH, cat. $NADP^+$, *i*PrOH, pH 5.5 buffer; (b) 1. $NaBH_4$, EtOH, 0 °C; 2. cat. *p*TsOH, toluene, room temp., 14 h, 120 °C, 4 h;[8] (c) 1. DIBAL-H, CH_2Cl_2, −78 °C; 2. *i*PrOH, PPTS, C_6H_6, 80 °C;[9] (d) TBAA, NMP, 85 °C; (e) K_2CO_3, MeOH, room temp.;[9] (f) PPh_3, imidazole, I_2, Et_2O/CH_3CN, 0 °C

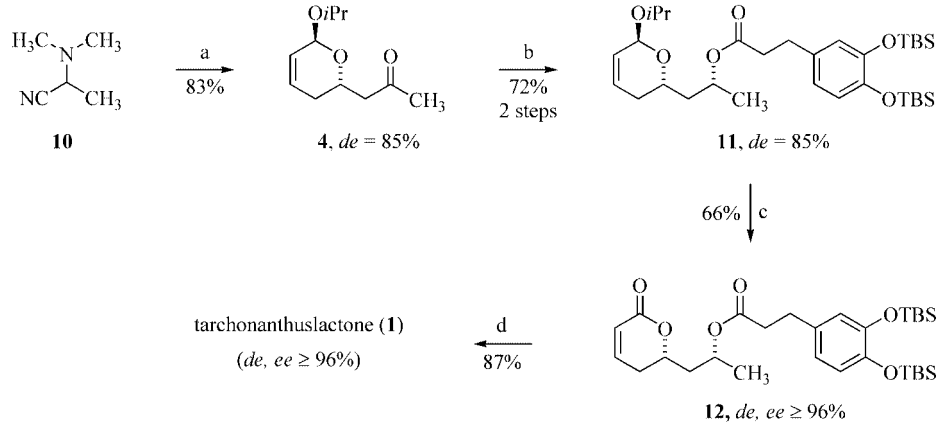
Because of the distinct indication of the sensitivity of α,β-unsaturated δ-lactone **5** towards decarboxylation in the course of the (*S*)-argentilactone and (*S*)-goniothalamin syntheses, the lactone moiety was protected by reduction and subsequent acetalization. This instability was also reported by Lichtenthaler et al., who used a similar lactone in their studies towards the total synthesis of (+)-anamarine.[11] The lactone moiety was therefore reduced with diisobutylaluminium hydride (DIBAL-H) in dichloromethane at low temperature, followed by pyridinium *p*-toluenesulfonate (PPTS) catalysed acetalization to provide the mixed acetal **7** in a good yield of 76% over two steps and with a diastereomeric excess of 85%.[9] As the lactone functionality has to be recovered by oxidation in one of the last steps of our synthesis, this stereocenter is lost, so there was no need to force the acetalisation reaction to complete diastereoselectivity.

However, efforts to convert the chloride **7** directly into the corresponding iodide **9** by a common Finkelstein reaction did not succeed at all.[12] It was therefore necessary first to synthesise the alcohol **8** and then to convert it into iodide **9**. The chloride **7** was transformed into its corresponding acetate by treatment with tetrabutylammonium acetate (TBAA) in *N*-methylpyrrolidone (NMP), and this was then converted into alcohol **8** by basic hydrolysis.[9] The yield of this two-step procedure was 93%. Direct iodination of alcohol **8** by treatment with triphenylphosphane, imidazole and iodine furnished the known compound **9** in a good yield of 82% (Scheme 2).[11,13]

The carbonyl group of the methyl ketone **4** could easily be introduced by the α-amino nitrile alkylation methodology and subsequent hydrolysis of the resulting α-amino nitrile product (Scheme 3).[14a−14g] The known acetaldehyde α-amino nitrile **10** was therefore deprotonated with lithium diisopropylamide (LDA) in tetrahydrofuran (THF).[15] Treatment with iodide **9** yielded the corresponding α-alkylation product, which was observed by NMR analysis of the crude product. During purification by column chromatography on silica gel, hydrolysis of the alkylated α-amino nitrile product occurred and the methyl ketone **4** could be directly isolated in a yield of 83% without the usual treatment with aqueous silver(I) nitrate or copper(II) sulfate (Scheme 3).

The chiral alcohol **2** was accessible by a chelate-controlled *syn*-selective reduction of the carbonyl group of methyl ketone **4** by treatment with L-selectride® as reducing agent in THF at −78 °C.[16a][16b] The secondary alcohol **2** was then directly treated with the doubly TBS-protected acid **3** in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) without any further purification to yield ester **11**. Acid **3** had previously been synthesized starting from caffeic acid by hydrogenation and TBS-protection by a literature method.[2d] The yield of the reduction/esterification procedure was 72% and a diastereomeric excess of only 43% was determined by ^{13}C NMR analysis. Obviously, the reduction of methyl ketone **4** (*de* = 85%) did not occur with complete diastereoselectivity. For this reason, the reduction was repeated in the same manner but at lower temperature (−100 °C) and in highly diluted solution. This time, NMR spectroscopic analysis of the ester **11** showed a diastereomeric excess of 85%, indicating that the carbonyl reduction had occurred with virtually complete diastereoselectivity.

In order to regenerate the α,β-unsaturated δ-lactone moiety, the ester **11** was treated with pyridinium chlorochromate (PCC) in dichloromethane to provide lactone **12** in an acceptable yield of 66% and with a diastereomeric excess greater than 96%. Possible racemization could be ruled out, because all analytical data, including the optical rotation of TBS-protected tarchonanthuslactone (**12**), corresponded to those reported by Solladié et al.[2d] Finally, deprotection of the aromatic hydroxy groups according to Solladié et al. by



Scheme 3. Reagents: (a) LDA, THF, 0 °C; 9, −78 °C to room temp.; SiO_2; (b) 1. L-Selectride®, CH_2Cl_2, −100 °C to room temp.; 2. DCC, DMAP, 3, CH_2Cl_2, room temp.; c) PCC, CH_2Cl_2, room temp.; (d) TBAF, benzoic acid, THF, room temp.

treatment of TBS-protected tarchonanthuslactone (**12**) with tetrabutylammonium fluoride (TBAF) and benzoic acid in THF furnished the target molecule tarchonanthuslactone (**1**) in a good yield of 87%.[2d] The synthesised title compound showed the same optical rotation ($[\alpha]_D^{28} = -80.8$, $c = 0.4$, $CHCl_3$) and analytical data as the natural product isolated from nature by Bohlmann et al.[1] or as synthesized by Solladié and co-workers.[2d]

Conclusion

An efficient and straightforward diastereo- and enantioselective synthesis of the polyketide natural product tarchonanthuslactone (**1**), based on the enantiomerically pure δ-lactone building block **5**, has been developed. A ten-step synthesis, involving a nucleophilic acylation through α-amino nitrile alkylation to obtain the methyl ketone **4** and its diastereoselective, chelate-controlled reduction, delivered the diastereo- and enantiomerically pure title compound in a good overall yield of 21%. Thanks to the availability of both enantiomers of the chloro lactone **5** through enzymatic reduction of *tert*-butyl 6-chloro-3,5-dioxohexanoate (**6**), the enantiomer of tarchonanthuslactone should also be accessible by the described procedure.

Experimental Section

General Remarks: All solvents were dried and purified prior to use. All reactions were carried out under atmospheres of argon. Column chromatography: Merck silica gel 60, 0.040−0.063 mm (230−400 mesh) (E = diethyl ether, PE = *n*-pentane). Optical rotation values: Perkin−Elmer P 241; solvents Merck Uvasol quality. IR: Perkin−Elmer FT/IR 1750. NMR: Varian VXR 300, Gemini 300, and Inova 400, TMS as internal standard. MS: Finnigan MAT 212 and Finnigan SSQ 7000 (70 eV). Microanalyses: Elementar vario EL. THF was dried by distillation from Na/Pb/benzophenone under an atmosphere of argon. Dichloromethane was distilled from calcium hydride under an atmosphere of argon. "Usual workup" means: (a) isolation of the organic layer, (b) extraction of the aqueous layer with diethyl ether or dichloromethane, (c) drying of the combined organic layers with $MgSO_4$, and (d) removal of the solvent under reduced pressure. The compositions of the stereoisomeric mixtures were determined by ^{13}C NMR spectroscopy.

Iodide 9: Imidazole (363 mg, 5.3 mmol), triphenylphosphane (1.322 g, 5.0 mmol), and iodine (949 mg, 3.7 mmol) were added at 0 °C to a solution of alcohol **8** (496 mg, 2.9 mmol) in a mixture of diethyl ether and acetonitrile (1.5:1.0, 62 mL). After stirring for 24 h at this temperature, the reaction mixture was diluted with diethyl ether (15 mL) and washed with $Na_2S_2O_3$ (10% wt. solution in water, 15 mL) and brine (15 mL). Drying with $MgSO_4$, filtration, and purification by column chromatography (PE/E, 8:1) gave 664 mg (82%) of iodide **9** as a colourless oil. $R_f = 0.70$ (PE/E, 4:1). $[\alpha]_D^{23} = +3.9$ ($c = 1.11$, $CHCl_3$). IR: $\tilde{\nu}$ = 2969, 2924, 2896, 1180, 1126, 1100, 1027 cm^{-1}. ^1H NMR: δ = 1.19 (d, $J = 6.2$ Hz, 3 H, $CHCH_3CH_3$), 1.26 (d, $J = 6.2$ Hz, 3 H, $CHCH_3CH_3$), 1.95−2.21 (m, 2 H, $CH{=}CHCH_2$), 3.23 (m, 2 H, CH_2I), 3.96 (m, 1 H, CH_2CHO), 4.15 [sept, $J = 6.2$ Hz, 1 H, $CH(CH_3)_2$], 5.11 (m, 1 H, $OCHO$), 5.72 (m, 1 H, $OCHCH{=}CH$), 5.99 (m, 1 H, $OCHCH{=}CH$) ppm. ^{13}C NMR: δ = 9.0 (CH_2I), 21.5 ($CHCH_3CH_3$), 23.8 ($CHCH_3CH_3$), 30.8 ($CH{=}CHCH_2$), 66.0 (CH_2CHO), 68.9 [$CH(CH_3)_2$], 92.8 ($CH{=}CHCH$), 126.1 ($CH{=}CHCH_2$), 127.6 ($CH{=}CHCH_2$) ppm. MS: *m/z* (%) = 183 (100) [$M^+ - 99$], 157 (6), 153 (5), 152 (17), 152 (17), 151 (5), 149 (7), 141 (5), 139 (22), 115 (6), 113 (11), 111 (7), 109 (6), 108 (8), 107 (13), 99 (5), 97 (10), 96 (10), 95 (10), 85 (9), 71 (15), 69 (16), 58 (10), 57 (26), 55 (14), 51 (14).

These analytical data correspond to those reported.[11]

Methyl Ketone 4: *n*-Butyllithium (15% wt. solution in *n*-hexane, 1.2 mL, 2.0 mmol) was added dropwise at 0 °C to a solution of diisopropylamine (198 mg, 2.0 mmol) in THF (14 mL). After the mixture had been stirred for 30 min at this temperature, amino nitrile **10** (194 mg, 2.0 mmol) was added. After stirring for another 30 min at this temperature, the reaction mixture was cooled to −78 °C. After slow addition of a solution of iodide **9** (460 mg, 1.6 mmol) in THF (14 mL), the reaction mixture was stirred for an additional 16 h and was then allowed to warm to room temperature. The reaction was quenched by addition of a saturated aqueous solution of $NaHCO_3$. The usual workup gave a residue, which was purified by column chromatography (PE/E, 4:1) to give 267 mg (83%) of methyl ketone **4** as a colourless oil. $R_f = 0.57$ (PE/E, 1:1). $[\alpha]_D^{23} = -17.8$ ($c = 1.02$, $CHCl_3$). IR: $\tilde{\nu}$ = 2971, 1381, 1127, 1102,

1085, 1022 cm^{-1}. ^1H NMR: δ = 1.17 (d, *J* = 6.1 Hz, 3 H, CHC*H*$_3$CH$_3$), 1.24 (d, *J* = 6.1 Hz, 3 H, CHCH$_3$C*H*$_3$), 2.02 (m, 2 H, CH=CHC*H*$_2$), 2.21 [s, 3 H, C(O)C*H*$_3$], 2.52 (dd, *J* = 15.5/4.5 Hz, 1 H, OCHC*H*H), 2.70 (dd, *J* = 15.5/8.2 Hz, 1 H, OCHCH*H*), 3.95 (q, *J* = 6.2 Hz, 1 H, OC*H*CH$_2$), 4.41 [sept, *J* = 4.6 Hz, 1 H, C*H*(CH$_3$)$_2$], 5.03 (d, *J* = 2.7 Hz, 1 H, CH=CHC*H*), 5.69 (m, 1 H, C*H*=CHCH$_2$), 5.97 (m, 1 H, CH=C*H*CH$_2$) ppm. ^{13}C NMR: δ = 21.5 (CH*C*H$_3$*C*H$_3$), 23.6 (CCH$_3$*C*H$_3$), 30.3 (CH=CH*C*H$_2$), 30.9 [C(O)*C*H$_3$], 49.3 (CHO*C*H$_2$), 63.0 [*C*H(CH$_3$)$_2$], 68.7 (O*C*HCH$_2$), 92.2 (CH=CH*C*H), 126.1 (*C*H=CHCH$_2$), 128.1 (CH=*C*HCH$_2$), 206.7 (*C*=O) ppm. MS: *m*/*z* (%) = 198 (1) [M$^+$], 140 (14), 139 (50), 138 (45), 112 (7), 100 (5), 99 (9), 97 (16), 96 (10), 95 (17), 82 (14), 81 (100), 79 (10), 71 (9), 70 (62), 68 (7), 67 (12), 57 (6), 53 (5). $C_{11}H_{18}O_3$ (198.26): calcd. C 66.64, H 9.15; found C 66.26, H 9.31.

Ester 11: L-Selectride® (1.0 M in THF, 1.3 mL, 1.3 mmol) was added dropwise at −100 °C over 30 min to a solution of methyl ketone **4** (100 mg, 0.5 mmol) in THF (170 mL). After the mixture had been stirred for 4 h at −78 °C the cooling bath was removed, and after 30 min the reaction was quenched by addition of water (50 mL). The usual workup gave a residue, which was filtered through a pad of silica gel (E). After evaporation of the solvent, the colourless oil was dissolved in dichloromethane (12 mL), acid **3** (308 mg, 0.8 mmol), DCC (155 mg, 0.8 mmol), and catalytic amounts of DMAP were added at room temperature, and the system was stirred for 2 h. The reaction mixture was diluted with diethyl ether (15 mL), filtered through a pad of Celite®, and concentrated in vacuo. The crude product was purified by column chromatography (PE/E, 10:1) to give 212 mg (72%, 2 steps) of ester **11** as a colourless oil. R_f = 0.29 (PE/E, 8:1). $[\alpha]_D^{22}$ = −8.7 (*c* = 1.02, $CHCl_3$). IR: $\tilde{\nu}$ = 2959, 2932, 2894, 2859, 1734, 1511, 1295, 1255, 1126, 1018, 908, 841, 783 cm^{-1}. ^1H NMR: δ = 0.17 [s, 6 H, Si(C*H*$_3$)$_2$], 0.18 [s, 6 H, Si(C*H*$_3$)$_2$], 0.98 (s, 9 H, *t*Bu), 0.99 (s, 9 H, *t*Bu), 1.14−1.26 (m, 9 H, CHC*H*$_3$CH$_3$, CHCH$_3$C*H*$_3$, OCHC*H*$_3$), 1.62 (m, 1 H, CHC*H*HCH), 1.94 [m, 3 H, CHCH*H*CH, C(O)C*H*$_2$], 2.52 (dd, *J* = 8.9/6.8 Hz, 2 H, CH=CHC*H*$_2$), 2.80 [t, *J* = 7.9 Hz, 2 H, C(O)CH$_2$C*H*$_2$], 3.99 (m, 2 H, OC*H*CH$_3$, CH$_2$C*H*OCH$_2$), 5.08 [m, 2 H, C*H*(CH$_3$)$_2$, C*H*CH=CH], 5.68 (ddd, *J* = 10.2/5.1/2.2 Hz, 1 H, CHCH=C*H*), 5.96 (m, 1 H, CHC*H*=CH), 6.61−6.76 (m, 3 H, Ph-*H*) ppm. ^{13}C NMR: δ = 4.1 [Si(*C*H$_3$)$_2$], 18.4 [*C*(CH$_3$)$_3$], 19.9 (C*C*H$_3$CH$_3$), 21.7 (CCH$_3$*C*H$_3$), 23.8 (OCH*C*H$_3$), 25.9 [C(*C*H$_3$)$_3$], 30.3 [C(O)CH$_2$*C*H$_2$], 30.6 [C(O)*C*H$_2$], 36.4 (CH=CH*C*H$_2$), 41.6 (OCH*C*H$_2$CHO), 63.2 (CH$_2$*C*HOCH$_2$), 68.0 [*C*H(CH$_3$)$_2$], 68.9 (O*C*HCH$_3$), 92.5 (O*C*HCH=CH), 120.9/121.1/121.2 (Ph-*C*$_{ortho,meta}$), 126.1 (OCHCH=*C*H), 128.4 (OCH*C*H=CH), 133.6 (Ph-*C*$_{ipso}$), 145.2/146.6 (Ph-*C*OSi), 172.4 (*C*=O) ppm. MS: *m*/*z* (%) = 592 (14) [M$^+$], 534 (11), 477 (7), 476 (16), 475 (46), 393 (10), 391 (6), 365 (5), 355 (9), 354 (5), 353 (66), 351 (16), 335 (8), 237 (8), 223 (7), 222 (12), 221 (80), 185 (7), 181 (10), 180 (15), 179 (100), 165 (6), 151 (8), 149 (8), 141 (18), 131 (12), 125 (5), 123 (50), 122 (9), 119 (5), 113 (11), 107 (5), 105 (7), 101 (5), 99 (19), 97 (8), 95 (22), 93 (11), 85 (5), 83 (8), 82 (5), 81 (48), 79 (6), 75 (6), 74 (5), 73 (90), 71 (17), 70 (6), 69 (19), 67 (7), 59 (13), 57 (17), 55 (17), 51 (5), 51 (24), 45 (37). $C_{32}H_{56}O_6Si_2$ (592.95): calcd. C 64.82, H 9.52; found C 64.97, H 9.58.

TBS-Protected Tarchonanthuslactone (12): Freshly ground PCC (230 mg, 1.0 mmol) was added at room temperature to a solution of ester **11** (103 mg, 0.2 mmol) in dichloromethane (4 mL) and the mixture was stirred for 3 h. The brown solid was removed by filtration, and the filtrate was concentrated in vacuo. The crude residue was purified by column chromatography (PE/E, 2:1 to 1:1) to give 63 mg (66%) of TBS-protected tarchonanthuslactone (**12**) as a colourless oil. R_f = 0.25 (PE/E, 1:1). $[\alpha]_D^{23}$ = −43.8 (*c* = 0.8, $CHCl_3$). ^1H NMR: δ = 0.18 [s, 6 H, Si(C*H*$_3$)$_2$], 0.19 [s, 6 H, Si(C*H*$_3$)$_2$], 0.98 (s, 9 H, *t*Bu), 0.99 [s, 9 H, C(C*H*$_3$)$_3$], 1.20 (d, *J* = 5.8 Hz, 3 H, CHC*H*$_3$), 1.94 (m, 1 H, CH=CHC*H*H), 2.15 (m, 1 H, CH=CHCH*H*), 2.25−2.40 (m, 2 H, C*H*$_2$CHCH$_3$), 2.56 (t, *J* = 7.6 Hz, 2 H, C*H*$_2$Ph), 2.81 [t, *J* = 7.6 Hz, 2 H, C(O)C*H*$_2$], 4.42 (m, 1 H, CH$_2$C*H*CH$_2$), 5.10 (m, 1 H, C*H*CH$_3$), 6.02 [d, *J* = 9.6 Hz, 1 H, C(O)C*H*=CH], 6.61−6.76 [m, 4 H, C(O)CH=C*H*, Ph-*H*] ppm. ^{13}C NMR: δ = −4.11 [Si(*C*H$_3$)$_2$], −4.07 [Si(*C*H$_3$)$_2$], 18.4 [*C*(CH$_3$)$_3$], 20.3 (OCH*C*H$_3$), 25.9 [C(*C*H$_3$)$_3$], 29.2 [C(O)CH$_2$*C*H$_2$], 30.2 [C(O)*C*H$_2$], 36.2 (CH=CH*C*H$_2$), 40.8 (OCH*C*H$_2$CHO), 67.1 (CH$_2$*C*HOCH$_2$), 74.9 (O*C*HCH$_3$), 120.9/121.1/121.2/121.4 [Ph-*C*$_{ortho,meta}$, C(O)*C*H=CH], 133.4 (Ph-*C*$_{ipso}$), 144.8 [C(O)CH=*C*H], 145.2/146.6 (Ph-*C*OSi), 164.0 [*C*(O)CH=CH], 172.5 [*C*(O)CH$_2$] ppm.

These analytical data correspond to those reported.[2d]

Tarchonanthuslactone (1): Benzoic acid (13 mg, 0.1 mmol) and TBAF (1.0 M solution in THF, 0.1 mL, 0.1 mmol) were added at room temperature to a solution of TBS-protected tarchonanthuslactone (**12**, 20 mg, 0.04 mmol) in THF (1.5 mL) and the mixture was stirred for 2 h. The reaction was quenched by addition of water (2 mL). The usual workup gave a residue, which was purified by column chromatography (E) to give 10 mg (87%) of tarchonanthuslactone (**1**) as a colourless solid. R_f = 0.30 (E). $[\alpha]_D^{28}$ = −80.8 (*c* = 0.4, $CHCl_3$). ^1H NMR: δ = 1.21 (d, *J* = 6.0 Hz, 3 H, CHC*H*$_3$), 1.78 (m, 1 H, CH=CHC*H*H), 2.10 (m, 1 H, CH=CHCH*H*), 2.15−2.35 (m, 2 H, C*H*$_2$CHCH$_3$), 2.62 (t, *J* = 6.9 Hz, 2 H, C*H*$_2$Ph), 2.85 [t, *J* = 6.9 Hz, 2 H, C(O)C*H*$_2$], 4.25 (m, 1 H, CH$_2$C*H*CH$_2$), 5.08 (m, 1 H, C*H*CH$_3$), 6.03 [d, *J* = 10.3 Hz, 1 H, C(O)C*H*=CH], 6.59 [m, 1 H, C(O)CH=C*H*], 6.70−6.86 (m, 3 H, Ph-*H*) ppm.

These analytical data correspond to those reported.[2d]

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